

**Statement
of
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on
VA Research on Alzheimer's Disease, Diabetes, and Parkinson's Disease,
before the
Subcommittee on Oversight and Investigations
of the
Committee on Veterans' Affairs
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Mr. Chairman and Members of the Subcommittee, I appreciate the opportunity to appear before you today to discuss the Department of Veterans Affairs' (VA) research into Alzheimer's disease, diabetes, and Parkinson's disease. VA research is committed to better understanding the causes and developing treatments and preventive measures for these diseases. Today, I would like to discuss the many achievements of VA research to help achieve this end.

Parkinson's Disease

Parkinson's Disease is a slowly progressive disorder that results from the degeneration of nerve cells in a small area of the midbrain that use the chemical dopamine to transmit information to other brain regions. Symptoms include tremors, slowness of movement, stiffness of the limbs, and problems with gait or balance. The symptoms interfere with employment and normal activities of daily living. The disease affects more than 500,000 Americans. The prevalence of Parkinson's disease increases with age; it affects 1% of the U.S. population over age 60 and 3.4% over age 74. Progress towards understanding the cause and cure of Parkinson's disease is crucially important to the population of aging veterans. Parkinson's disease affects thousands of veterans and creates an enormous burden on patients and their families. VA medical centers treat over 40,000 Parkinson's disease patients every year. At present there is no cure for Parkinson's disease, but treatments do exist and are

available. Despite advances in treatment, relentless progression of neuronal damage frequently leads to total disability. Further research into fundamental mechanisms of neuronal degeneration is the best hope for the development of improved diagnostic and treatment regimens.

The four Research Services of VA's Office of Research and Development, Biomedical Laboratory Research & Development Service (BLR&D), Clinical Science Research & Development Service (CSR&D), Health Services Research & Development Service (HSR&D), and Rehabilitation Research & Development Service (RR&D), have made funding for innovative studies focused on the pathogenesis and treatment of Parkinson's disease a high priority. Over the past five years, VA funding for Parkinson's disease research has nearly doubled, with \$10.1 million allocated for projects in FY 2004. Since FY 1999, non-VA funding has more than doubled, with VA investigators leveraging over \$6.4 million in non-VA funds in FY 2003. The funded projects focus on various aspects of Parkinson's disease research, including:

- the role of neurotransmitters other than dopamine,
- advances in neuroimaging technologies to monitor disease progression,
- stem cell and fetal transplantation research in animal models,
- gene therapy in animal models,
- mechanisms of damage to nerve cells,
- non-motor aspects of Parkinson's disease,
- rehabilitative strategies for Parkinson's disease, and
- clinical trials of surgical treatment for refractive Parkinson's disease.

With the development of six Parkinson's Disease Research, Education and Clinical Centers (PADRECCs), initiated in FY 2001, VA took a major step toward improving patient care and outcomes while, over the longer term, pursuing a cure for Parkinson's disease. Operating together as a national consortium, the PADRECCs conduct research covering basic biomedicine, rehabilitation, health services delivery, and clinical trials. Each Center is participating in a landmark clinical trial with the Cooperative Studies Program (CSP) that began in November 2001 to assess the

effectiveness of surgical implantation of deep brain stimulators (DBS) in reducing the symptoms of Parkinson's disease.

In collaboration with the National Institutes of Health's (NIH) National Institute for Neurological Disorders and Stroke, the DBS trial on Parkinson's disease is investigating a promising neurosurgical technique utilizing implantation of electrical stimulation devices, in comparison to best medical therapy, to assess the impact on symptoms and functioning of Parkinson's patients. This study will be the largest trial to assess the effectiveness of DBS to treat refractory Parkinson's disease. There are two components to this study, a comparison of best medical therapy to DBS, and a comparison of stimulation at two locations on patient outcomes (simultaneous bilateral subthalamic nuclei stimulation (STN) and simultaneous bilateral globus pallidus (GPi) stimulation). The objective of the "stimulation" component, assessed at two years following surgery, is to determine at which location is stimulation more effective in attenuating symptoms of Parkinson's disease at the end of the two-year period. The objective of the "medical therapy" component is to determine whether DBS or best medical therapy is more effective at six months in improving Parkinson's disease motor symptoms. The primary study endpoint for comparison of surgical site (STN vs. GPi DBS) is a widely accepted standard clinical scale for evaluating individuals with Parkinson's disease (the motor subscale of the Unified Parkinson's disease Rating Scale). For the comparison of best medical therapy to DBS, the primary endpoint will be time spent without having difficulties in performing voluntary movements on patient motor diaries. The study is planned to continue until 2007. As of April 2004, 138 patients have enrolled.

In addition to the DBS trial, the PADRECCs are implementing a prospective patient care registry as a means of monitoring the care of veterans. No such clinical Parkinson's disease registry has been previously established on a national scale. The anticipated benefits are the improvement of clinical care by tracking the clinical status and interventions of veterans with Parkinson's disease. The PADRECCs were also recently involved in a study to determine the indicators of quality health care for persons with Parkinson's disease. Using a literature review, followed by input from expert Parkinson's clinicians, a series of indicators were established, published, and distributed

throughout the VA health care system. Numerous bench research projects, clinical trials, clinical demonstrations and rehabilitation projects are also underway at the individual PADRECCs.

RR&D has recently funded several studies on rehabilitative strategies for Parkinson's disease. RR&D investigators are working to develop a valid method for measuring and interpreting the energy costs of activities of daily living for persons with physical impairments, including Parkinson's disease. They are utilizing body weight supported treadmill training to research re-teaching the body the proper gait patterns following trauma and during disease processes that compromise the ability to walk. They are also evaluating neurobiological and postural control mechanisms underlying the risk of falling in elderly veterans. In addition, RR&D investigators are studying the application of magnetic energy (accelerated Transcranial Magnetic Stimulation) to lessen depression and alleviate motor symptoms of Parkinson's disease.

Diabetes

Diabetes is one of the leading causes of disability and death in the U.S. Approximately 18 million people have diabetes mellitus, and each year over one million more people over the age of 20 develop the disease. By the year 2025, it is predicted that nearly 10% of our population will have diabetes.

VA is the largest integrated healthcare system in the U.S. providing care to people with diabetes. One in six veterans have this disease, and veterans with diabetes account for nearly 25% of all VA pharmacy costs and for more than 1.7 million hospital bed days of care annually. Diabetes affects nearly 20% of veterans receiving care in the VA healthcare system and is a leading cause of microvascular complications, such as blindness, end stage renal disease, and amputation. Moreover, middle-aged persons with diabetes have two to four times the risk of coronary artery disease and stroke compared to similar persons without diabetes.

All four Research Services of the Office of Research and Development have made funding for diabetes research a high priority. Over the past five years, VA funding for diabetes research has increased to over \$16.8 million in FY 2004. Since FY 1999, non-VA funding has grown by more than \$13 million with VA investigators now

leveraging over \$35.8 million in non-VA funds in FY 2003. Some of the areas of research include:

- diabetes-related complications in aging and effects of exercise and diet,
- regulation of glucose transporters and gene transcription by insulin and glucose,
- pathogenesis and genetics of diabetic neuropathy and diabetic retinopathy,
- molecular mechanism of insulin resistance,
- linkage analysis and genetic studies of type-2 diabetes,
- islet transplantation studies, and
- rehabilitative strategies for Diabetes.

CSP is currently conducting a large-scale trial to determine if intensified blood-sugar control and management reduces major vascular complications that lead to most deaths, illnesses and treatment costs for type-2 diabetic patients. Patients will receive either standard diabetic drug therapy or an enhanced, additive therapy regimen designed to maintain tight control over blood sugar levels. Patient accrual for this study was completed in May 2003, with 1792 patients from 20 VA sites being randomized for participation. This study began in May 2000 and has a targeted completion date in 2008, after a 5-year patient follow-up.

We have seen great improvements in the quality of care and health outcomes of veterans with diabetes as a result of the HSR&D Diabetes Mellitus Quality Enhancement Research Initiative (QuERI) in Ann Arbor, MI. The Diabetes Mellitus QuERI is part of a VHA-wide effort to improve the quality of patient care in ways that are measurable, rapid and sustainable. It is charged with identifying and evaluating diabetes care practices, current gaps in care, and interventions to improve care and patient outcomes for veterans with diabetes. The Diabetes QuERI has several objectives and is concentrating on a number of areas highlighted within the VHA/DOD clinical practice guidelines, including glycemic control, hyperlipidemia, hypertension, and screening and early intervention for retinopathy and foot complications. The Diabetes QuERI can facilitate the implementation of interventions and care processes that are most likely to produce substantial improvements in the quality and length of life

for many veterans with diabetes as well as promote the most efficient use of VA resources.

Recent accomplishments of the Diabetes Mellitus QuERI in clinician and patient education, as well as clinical practice support tools include:

- development of educational briefs on glycemic, blood pressure and lipid control,
- development of a brochure that translates the *National VHA Diabetes Clinical Guidelines* into lay language for distribution to veterans with type-2 diabetes,
- creation of personalized diabetes profile worksheets that use the patients own test results to assist them in understanding the recommendations in the *National VHA Diabetes Clinical Guidelines* and to facilitate goal setting,
- participation in registry development for diabetes patients with high risk feet, and
- development of a patient survey instrument and organizational assessment tool for diabetes patients at high risk for amputation.

HSR&D has recently funded several other studies with significant impacts. Investigators have shown that VA facilities with higher levels of programming coordination and feedback coordination have significantly lower foot amputation rates. They have also demonstrated that improved blood pressure control in patients with type-2 diabetes leads to substantially reduced risks of cardiovascular events and mortality. Additionally, they have shown that physicians' communication and participatory decision-making style were both strongly associated with patients' reported diabetes self-management.

In BLR&D and CSR&D, several studies are underway examining the causes, pathogenesis and treatment of Diabetes. VA researchers have just completed the largest prospective epidemiological study to date comparing auditory function in diabetic and non-diabetic veterans. Preliminary results indicate that significantly poorer hearing exists in diabetic veterans compared to non-diabetic veterans 60 years of age or younger, but no significant difference exists in the two groups over 60 years old. These results may bring about changes in the standard of care provided to diabetic patients, including routine hearing tests to reveal changes in hearing status. Other investigators

are exploring the effects of physical activity, body weight and genetics on Diabetes aimed ultimately at improving treatments for veterans with Diabetes.

Investigators in RR&D are researching rehabilitative strategies for diabetic patients. They are involved in the developmental testing and enhancement of VA Pedorthic Computer-aided Design and Computer-aided Manufacturing (CAD/CAM) of orthopedic footwear to alleviate painful and debilitating conditions of the feet associated with diabetes. They are also evaluating the efficacy of a telerehabilitation system designed to improve post-discharge care to veterans who have had a recent lower limb amputation or who have a leg or foot ulcer. In addition, RR&D researchers are examining how somatic sensory dysfunction contributes to slips and falls in an older, diabetic population.

Alzheimer's Disease

Alzheimer's disease is a complex illness that causes the gradual loss of brain cells. Although the disease was once considered rare, research has now shown that it is the leading cause of dementia. Approximately 4.5 million Americans have this disease, and it is a major cause of morbidity and mortality among veterans. Although many things about Alzheimer's remain a mystery, research continues to bring us a better understanding of the disease, more accurate diagnoses, and more effective treatments.

VA supports a broad array of studies related to Alzheimer's disease. Over the past five years, VA funding for Alzheimer's disease research has increased to over \$6.3 million in FY 2004. Since FY 1999, non-VA funding has increased by over \$12 million to nearly \$42.8 million in FY 2003. Some of the areas of research include:

- vaccine development for Alzheimer's disease,
- advances in neuroimaging technologies to monitor disease progression,
- gene therapy in animal models,
- mechanisms of damage to nerve cells,
- inflammatory mechanisms in Alzheimer's disease,
- gene–Environment interactions in Alzheimer's disease, and
- therapeutic interventions.

Investigators in BLR&D and CSR&D are working on developing non-invasive techniques that would allow early identification of patients with Alzheimer's disease prior to the onset of severe memory loss or other cognitive deficits. Investigators are also working with imaging technologies to discover ways to easily monitor the disease progression and response to therapy. Other VA researchers are involved in a project to develop an Alzheimer's disease vaccine and are examining the potential of other pharmaceutical interventions.

HSR&D has also recently funded several significant studies on the quality of care and outcomes of veterans with Alzheimer's disease. Investigators demonstrated that veterans with dementia who receive appropriate interventions from caregivers might be able to remain at home longer in environments that promote maximum independence for both caregivers and patients.

HSR&D researchers have also revealed a significant relationship between discomfort and agitation among nursing home residents with dementia, suggesting that agitated behaviors may be associated with increased pain. Accordingly, better quality of life for long-term care residents may result from regularly scheduled pain management. In addition, researchers are working to help provide an environmentally safe home living situation for veterans with dementia by giving caregivers the know-how and self-confidence to prevent risky behavior that leads to injuries.

Among other studies, RR&D is working in partnership with the Rosalynn Carter Institute (RCI) for Human Development on two exciting initiatives. RR&D is a member of the National Quality Caregiving Coalition (NQCC), a group sponsored by RCI. RCI, in collaboration with RR&D and other interested groups, is developing a national report card on care giving in America. Work on the report card is in its initial planning stages to define the pertinent variables to be included and questions to be asked. RR&D will be involved in all stages of this project. RR&D is also taking the lead in planning a joint research project between the Atlanta VAMC and RCI to examine a caregiver intervention program. This effort involves RR&D central office research staff, central office clinical care staff, VAMC Atlanta clinician scientists and RCI staff.

Four exciting projects examining new potential treatments for Alzheimer's disease will be reviewed this June for funding in FY 2005. Two of these projects examine the effectiveness of ibuprofen and other non-steroidal anti-inflammatory drugs (NSAIDS) to preserve cognitive function and prevent the pathological damage. The third project examines the efficacy of an herbal supplement component reported to be a memory enhancer and natural therapy for Alzheimer's disease. The last project examines two potential Alzheimer Disease therapies: immunization/vaccine development and cholesterol lowering drugs (statins).

We are very proud of VA's accomplishments in Parkinson's disease, Diabetes and Alzheimer's disease research, and we remain committed to maintaining the highest quality research in the country to best serve the needs our nation's veterans.

Mr. Chairman, this concludes my statement. I will now be happy to answer any questions that you and other members of the Subcommittee might have.